

IN THE CLAIMS

1. (Previously Amended) A nucleic acid molecule that comprises or that encodes, in 5' to 3' order, a first region of interest, a first base-paired region, a loop region, and a second base-paired region, wherein said first and second base-paired regions are capable of base-pairing to each other or are base-paired to each other.
2. (Previously Amended) The nucleic acid molecule of claim 1, further comprising a second region of interest downstream of said second base-paired region, wherein said first and second regions of interest are capable of base-pairing to each other or are base-paired to each other.
3. (Original) The nucleic acid molecule of claim 2, wherein said first and second regions of interest differ in length.
4. (Original) The nucleic acid molecule of claim 2, wherein said first region of interest has substantial identity to a region of a target gene and said second region of interest has substantial complementarity to said target gene, and wherein said nucleic acid molecule inhibits expression of said target gene in a cell.
5. (Original) The nucleic acid molecule of claim 4, wherein said first region of interest has substantial identity to a region of two or more target genes, and said second region of interest has substantial complementarity to said region of said two or more target genes, and wherein said nucleic acid molecule inhibits expression of said two or more target genes in a cell.
6. (Original) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises deoxyribonucleotides, ribonucleotides, or a mixture thereof.
7. (Original) The nucleic acid molecule of claim 4, wherein said target gene is a nucleic acid molecule associated with a disease or disorder, a bacterial infection, a viral infection, a yeast infection, or double-stranded ribonucleic acid (dsRNA)-mediated toxicity, or encodes a bacterial

polypeptide, a viral polypeptide, a yeast polypeptide, a polypeptide associated with a disease or disorder, or a polypeptide associated with double-stranded ribonucleic acid (dsRNA)-mediated toxicity.

8. (Original) The nucleic acid molecule of claim 7, wherein said polypeptide associated with a disease or a disorder is a cancer-causing polypeptide.

9. (Canceled)

10. (Previously Amended) The nucleic acid molecule of claim 1, wherein said first region of interest is at least 1 to 1000 nucleotides.

11. (Previously Amended) The nucleic acid molecule of claim 2, wherein said first and second base-paired regions are complementary to each other and not to said target gene.

12-15. (Canceled)

16. (Previously Amended) The nucleic acid molecule of claim 10, wherein said first region of interest is at least 19 to 26 nucleotides.

17. (Previously Amended) The nucleic acid molecule of claim 10, wherein said first region of interest is at least 15 to 25 nucleotides.

18. (Canceled)

19. (Previously Amended) The nucleic acid molecule of claim 2, wherein said second region of interest is at least 1 to 1000 nucleotides.

20-24. (Canceled)

25. (Previously Amended) The nucleic acid molecule of claim 19, wherein said second region of interest is at least 19 to 26 nucleotides.

26. (Previously Amended) The nucleic acid molecule of claim 19, wherein said second region of interest is at least 15 to 25 nucleotides.

27-32. (Canceled)

33. (Previously Amended) The nucleic acid molecule of claim 1, wherein said first base-paired region is at least 1 to 50 nucleotides.

34-35. (Canceled)

36. (Previously Amended) The nucleic acid molecule of claim 33, wherein said first base-paired region is at least 5 to 15 nucleotides.

37-41. (Canceled)

42. (Previously Amended) The nucleic acid molecule of claim 1, wherein said second base-paired region is at least 1 to 50 nucleotides.

43-44. (Canceled)

45. (Previously Amended) The nucleic acid molecule of claim 42, wherein said second base-paired region is at least 5 to 15 nucleotides.

46. (Previously Amended) The nucleic acid molecule of claim 1, wherein said first and second base-paired regions are the same length.

47-53. (Canceled)

54. (Previously Amended) The nucleic acid molecule of claim 1, wherein said loop region is at least 5 to 15 nucleotides.

55. (Original) A pharmaceutical composition comprising the nucleic acid molecule of claim 1 and a pharmaceutically acceptable carrier or diluent.

56. (Previously Amended) A pharmaceutical composition comprising a vector construct comprising, at the 5' end, a promoter that is operably linked to a nucleic acid molecule and which enables transcription of said nucleic acid molecule, wherein said nucleic acid molecule encodes, in 5' to 3' order, a first region of interest, a first base-paired region, a loop region, and a second base-paired region, wherein said first and second base-paired regions are capable of base-pairing to each other, and wherein transcription of said nucleic acid molecule produces an RNA hairpin.

57. (Previously Amended) A method for generating an RNA hairpin comprising transcribing a nucleic acid molecule in a host cell that has been transformed with said nucleic acid molecule, wherein said nucleic acid molecule comprises, at the 5' end, a promoter that is operably linked to said nucleic acid molecule and which enables transcription of said nucleic acid molecule, and wherein said nucleic acid molecule encodes, in 5' to 3' order, a first region of interest, a first base-paired region, a loop region, and a second base-paired region, wherein said first and second base-paired regions are capable of base-pairing to each other, wherein transcription of said nucleic acid molecule produces an RNA hairpin.

58. (Previously Amended) The method of claim 57, wherein said nucleic acid molecule further encodes a second region of interest downstream of said second base-paired region, wherein said first and second regions of interest are capable of base-pairing to each other.

59. (Previously Amended) The method of claim 58, wherein the 5' end of said RNA hairpin comprising the first region of interest and the 3' end of said RNA hairpin comprising the second region of interest are base-paired and partially overlap to form a partial RNA hairpin having a

non-overlapping region, wherein the 5' end of said first region of interest extends beyond the 3' end of said second region of interest.

60. (Previously Amended) The method of claim 58, wherein the 5' end of said RNA hairpin comprising the first region of interest and the 3' end of said RNA hairpin comprising the second region of interest are base-paired and partially overlap to form a partial RNA hairpin having a non-overlapping region, wherein the 3' end of said second region of interest extends beyond the 5' end of said first region of interest.

61. (Original) The method of claim 59, wherein said non-overlapping region of said partial RNA hairpin is extended in vivo by an RNA-dependent RNA polymerase.

62. (Original) The method of claim 61, wherein said RNA-dependent RNA polymerase is endogenous to said host cell.

63. (Original) The method of claim 61, wherein said RNA-dependent RNA polymerase is exogenous to said host cell and is provided to said host cell.

64. (Previously Amended) A method for inhibiting the expression of a target gene in a cell, said method comprising administering to a subject in need thereof, a nucleic acid molecule that comprises or that encodes an RNA hairpin, wherein said RNA hairpin comprises, in 5' to 3' order, a first region of interest, a first base-paired region, a loop region, a second base-paired region, and a second region of interest, wherein said first and second base-paired regions are capable of base-pairing to each other or are base-paired to each other, and wherein said administering inhibits or reduces expression of a target gene, relative to expression of said target gene in a subject not administered said nucleic acid molecule.

65. (Original) The method of claim 64, wherein said first and second regions of interest are the same or different lengths.

66. (Previously Amended) The method of claim 65, wherein the 5' end of said RNA hairpin comprising the first region of interest and the 3' end of said RNA hairpin comprising the second region of interest are base-paired and partially overlap to form a partial RNA hairpin having a non-overlapping region, wherein the 5' end of said first region of interest extends beyond the 3' end of said second region of interest.

67. (Previously Amended) The method of claim 65, wherein the 5' end of said RNA hairpin comprising the first region of interest and the 3' end of said RNA hairpin comprising the second region of interest are base-paired and partially overlap to form a partial RNA hairpin having a non-overlapping region, wherein the 3' end of said second region of interest extends beyond the 5' end of said first region of interest.

68. (Original) The method of claim 66, wherein said non-overlapping region of said partial RNA hairpin is extended in vivo by an RNA-dependent RNA polymerase.

69. (Original) The method of claim 68, wherein said RNA-dependent RNA polymerase is endogenous to said host cell.

70. (Original) The method of claim 68, wherein said RNA-dependent RNA polymerase is exogenous to said host cell and is provided to said host cell.

71. (Original) The method of claim 64, wherein said first region of interest has substantial identity to a region of said target gene and said second region of interest has substantial complementarity to said target gene, and wherein said nucleic acid molecule inhibits expression of said target gene in a cell of said subject.

72. (Previously Amended) The method of claim 71, wherein said first region of interest has substantial identity to a region of two or more target genes, and said second region of interest has substantial complementarity to said region of said two or more target genes, and wherein said nucleic acid molecule inhibits expression of said two or more target genes in a cell of said

subject.

73. (Original) The method of claim 71, wherein said target gene is a nucleic acid molecule associated with a disease or disorder, a bacterial infection, a viral infection, a yeast infection, or double-stranded ribonucleic acid (dsRNA)-mediated toxicity, or encodes a bacterial polypeptide, a viral polypeptide, a yeast polypeptide, a polypeptide associated with a disease or disorder, or a polypeptide associated with double-stranded ribonucleic acid (dsRNA)-mediated toxicity.

74. (Original) The method of claim 73, wherein said polypeptide associated with a disease or a disorder is a cancer-causing polypeptide.

75. (Previously Amended) The nucleic acid molecule of claim 64, wherein said first and second base-paired regions are complementary to each other and not to said target gene.

76. (Previously Amended) The method of claim 64, wherein inhibiting the expression of said target gene is used to treat, stabilize, or prevent infection in an animal.

77-87. (Canceled)

88. (Previously Amended) The method of claim 64, wherein inhibiting the expression of said target gene is used to treat or prevent cancer.

89-116. (Canceled)

117. (New) A genetic construct comprising two or more promoter-loop region-termination site expression units.

118. (New) The genetic construct of claim 117, wherein each expression unit further comprises a first region of interest between said promoter and said loop region, wherein said first

region of interest comprises a sequence of substantial identity or complementarity to a target gene.

119. (New) The genetic construct of claim 118, further comprising a gene encoding an RNA-dependent RNA polymerase (RdRp).

120. (New) The genetic construct of claim 118, wherein each expression unit further comprises a second region of interest between said loop region and said termination site, wherein said first and second regions of interest are capable of base-pairing to each other.

121. (New) The genetic construct of claim 120, wherein said each expression unit encodes a double stranded RNA (dsRNA) that is at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 nucleotides in length.

122. (New) The genetic construct of claim 121, wherein at least 50% of the nucleotides in said first and second regions of interest participate in Watson-Crick base-pairing with each other.

123. (New) The genetic construct of claim 122, wherein at least 70% of the nucleotides in said first and second regions of interest participate in Watson-Crick base-pairing with each other.

124. (New) The genetic construct of claim 123, wherein at least 90% of the nucleotides in said first and second regions of interest participate in Watson-Crick base-pairing with each other.



125. (New) The genetic construct of claim 124, wherein at least 95% of the nucleotides in said first and second regions of interest participate in Watson-Crick base-pairing with each other.

126. (New) The genetic construct of claim 125, wherein 100% of the nucleotides in said first and second regions of interest participate in Watson-Crick base-pairing with each other.

127. (New) The genetic construct of claim 117, wherein at least one promoter is a polIII promoter.

128. (New) The genetic construct of claim 117, wherein at least one termination site is a polIII termination site.

129. (New) The genetic construct of claim 117, wherein each unit further comprises a first multiple cloning site (MCS) between the promoter and loop region.

130. (New) The genetic construct of claim 129, wherein each unit further comprises a first region of interest inserted at said first MCS, wherein said first region of interest comprises a sequence of substantial identity or complementarity to a target gene.

131. (New) The genetic construct of claim 129, wherein each unit further comprises a second MCS between the loop region and termination site.

132. (New) The genetic construct of claim 131, wherein a second region of interest is inserted at said second MCS, wherein said first and second regions of interest are capable of base-pairing to each other.

133. (New) The genetic construct of claim 117, wherein each unit further comprises in 5' to 3' order, a promoter, a first base-paired region, a loop region, a second base-paired region and a termination site, wherein said first and second base-paired regions are capable of base-pairing to each other.

134. (New) The genetic construct of claim 133, wherein each unit further comprises a first region of interest between said promoter and said first-base-paired region, wherein said first region of interest comprises a sequence of substantial identity or complementarity to a target gene.

135. (New) The genetic construct of claim 134, further comprising a gene encoding an RNA-dependent RNA polymerase (RdRp).

136. (New) The genetic construct of claim 134, wherein each expression unit further comprises a second region of interest between said second base-paired region and said termination site, wherein said first and second regions of interest are capable of base-pairing to each other.

137. (New) The genetic construct of claim 133, wherein each unit further comprises a first multiple cloning site (MCS) between the promoter and first base-paired regions.

138. (New) The genetic construct of claim 137, wherein each unit further comprises a first region of interest inserted at said first MCS, wherein said first region of interest comprises a sequence of substantial identity or complementarity to a target gene.

139. (New) The genetic construct of claim 137, wherein each unit further comprises a second MCS between the second base-paired region and termination site.

140. (New) The genetic construct of claim 139, wherein a second region of interest is inserted at said second MCS, wherein said first and second regions of interest are capable of base-pairing to each other.

141. (New) A composition comprising an at least partially double stranded multiple epitope dsRNA comprising non-contiguous dsRNA segments with substantial identity to one or multiple target genes.

142. (New) The composition of claim 141, wherein said multiple epitope dsRNA inhibits the expression of two or more target genes.

143. (New) The composition of claim 142, wherein said target genes are pathogen genes.

144. (New) The composition of claim 142, wherein said target genes are oncogenes.

145. (New) The composition of claim 141, wherein said segments with substantial identity to a target gene are at least 30, 40, 50, 100, 200, 500, 750 or more nucleotides in length.

146. (New) The composition of claim 141, wherein at least 50% of the nucleotides in said dsRNA segments participate in Watson-Crick base-pairing with each other.

147. (New) The composition of claim 146, wherein at least 70% of the nucleotides in said dsRNA segments participate in Watson-Crick base-pairing with each other.

148. (New) The composition of claim 147, wherein at least 90% of the nucleotides in said dsRNA segments participate in Watson-Crick base-pairing with each other.

149. (New) The composition of claim 148, wherein at least 95% of the nucleotides in said dsRNA segments participate in Watson-Crick base-pairing with each other.

150. (New) The composition of claim 149, wherein 100% of the nucleotides in said dsRNA segments participate in Watson-Crick base-pairing with each other.

151. (New) A DNA construct encoding the multiple epitope dsRNA of claim 141.

152. (New) A method for inhibiting the expression of one or more target genes in a cell comprising introducing into said cell the genetic construct of claim 117.

153. (New) A method for inhibiting the expression of one or more target genes in a cell comprising introducing into said cell the composition of claim 141.

154. (New) A method for inhibiting the expression of one or more target genes in a cell comprising introducing into said cell the DNA construct of claim 151.